6. The method of claim 1 wherein said method comprises using the technique referred to as in situ hybridization.

Remarks:

Claim 1 has been amended. New claim 6 has been added. Support for these amendments may be found in the specification at the following pages; no new matter has been added:

Claim 1- support at page 10; lines 17-18;
Claim 6- support at page 10, lines 18-20; page 11, lines 16-20.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Claims 1 and 2 have been rejected under 35 U.S.C. 112, first paragraph, because, while the specification enables methods of detecting breast tumors, the Examiner states that it does not enable detection of "any type of tumor". In response, Applicants have amended Claim 1 to specify detection of a breast tumor.

Claims 1 and 2 have been rejected under 35 U.S.C 102(e) in light of Papsidero et al., US Patent 6,306,653 (hereafter "Papsidero").

According to the Examiner, Papsidero teaches a nucleic acid sequence and the use of nucleic acid probes from the nucleic acid sequence for use in the detection of breast cancer and "[t]hus, Papsidero teaches methods that are the same as that claimed" (Office Action at page 4). However, given an analysis of the data disclosed in the instant application and what is disclosed in Papsidero, Applicants respectfully disagree.

Applicants respectfully submit that Papsidero discloses a method of detecting breast disease in a patient based on the theory that diseased (i.e. cancerous) breast cells produce increased levels of the novel chemokine referred to as "MACK" (referred to by Applicants as "MEC", hereafter "MACK/MEC"). As such, Papsidero teaches detecting breast tumors based on the **presence** of this protein or mRNA levels thereof, in sera or tissue samples from a patient. For example:

> The nucleic acid molecules which hybridize under stringent conditions to nucleic acid molecules encoding a chemokine of the present invention can be used as probes in hybridization assays to detect breast disease in a patient. For example, a sample of tissue or body fluid from the patient is contacted with a nucleic acid probe which, under stringent conditions, hybridizes to a nucleic acid molecule encoding a chemokine according to the present invention or a complement thereof. The contacting is carried out under conditions effective to permit formation of a hybridization complex between the probe and breast tissue specific nucleic acid molecules (i.e., the nucleic acid molecules encoding chemokines of the present invention). Breast disease is then detected by detecting the hybridization complex.

Papsidero, column 19, lines 58-67, column 20 lines 1-4.

Applicants respectfully submit that despite making the assumption that MACK/MEC may be detected in diseased breast tissue, Papsidero does not provide extensive or compelling data regarding expression levels in breast tissue. Instead, the reference's real focus is on increased levels of MACK/MEC in the sera of breast cancer patients and how "detection of these immunoreactivities can be of diagnostic and/or monitoring value for the disease" (Papsidero, column 35, lines 55-57 and Table 6, column 36). Indeed, while presenting data based on the analysis of cultured cells, sera from breast cancer patients and normal breast tissue, Papsidero actually only discloses data from one cancerous breast tissue sample -an invasive ductal carcinoma of the breast- and without proper controls (Papsidero, Table 4, column 33). Nevertheless, based on this one uncontrolled data point, Papsidero concludes that the MACK/MEC chemokine is expressed and detectable in cancerous breast tissue.

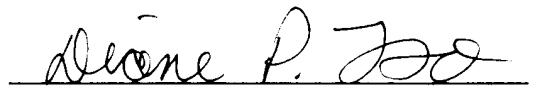
While levels of MACK/MEC may indeed be increased in the serum of a breast cancer patient (perhaps along with other breast specific proteins released due to the neovascularization which occurs during tumorigenesis), surprisingly, in contrast to Papsidero, Applicant's carefully controlled data indicates that the MACK/MEC chemokine is actually ***not*** expressed in cancerous breast epithelium. In contrast to Papsidero, the instant invention discloses extensive Northern blot analysis as well as in situ hybridization data with antisense and sense MEC/MACK riboprobes using many samples of matched tumor and normal breast tissue, i.e., Applicants analyzed MACK/MEC expression in cancerous breast tissue and compared to expression levels in normal breast tissue from the same patient. Based on these carefully analyzed data (which have been subjected to peer review; see *Mickanin, C. et al., International Journal of Oncology 18: 939-944, 2001* a copy of which is attached for the Examiner's convenience), Applicants claim a diagnostic method which comprises

detecting the ***under expression*** of MACK/MEC levels in breast tumors. As such, Applicants respectfully submit that Papsidero clearly does not teach methods that are the same as that claimed in the instant application.

In view of the forgoing, Applicants respectfully request that a timely Notice of Allowance be issued in this case.

If there are any fees due in connection with this communication, including any fees for a required extension of time, such an extension is requested and the Commissioner is authorized to charge the fees to Deposit Account No. 19-0134 in the name of Novartis.

Respectfully submitted,



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Date: January 16, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claim 1 has been amended as follows:

1. (Amended) A method for detecting a breast tumor, comprising the steps of:

   a) providing a probe containing a polynucleotide which comprises the sequence of SEQ ID NO:1 or a fragment thereof;

   b) contacting said probe to a sample of ~~body fluid~~ tissue or tissue extract from a patient under a hybridizing condition to produce a hybridized probe; and

   c) quantifying the level of hybridization with said probe wherein suppressed hybridization compared to control levels indicate the presence of a breast tumor.

Claim 6 has been added:

6. The method of claim 1 wherein said method comprises using the technique referred to as in situ hybridization.